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BLASTOMYCOSIS AND SOME OTHER CONDITIONS DUE TO YEAST-LIKE FUNGI (BUDDING FUNGI)[1]

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The term Blastomycosis *sensu lato* covers all conditions due to yeast-like fungi but from a practical point of view it is of advantage—as it is usually done in this country—to limit its meaning to denote solely or principally a clinical entity or, more correctly, a group of closely allied entities characterized by the presence of granulomatous, verrucoid lesions in which fungi of the type *Blastomycoides* are found.

Yeast-like fungi. The term "yeast-like fungi" or "budding fungi" is unscientific, but useful in practice. "Yeast-like fungi" are fungi which in the lesions appear as free oval or roundish cells, some of them budding, with usually no mycelium at all, exceptionally a few mycelial elements. In cultures there may be only budding cells, or budding cells and mycelium or mycelia only. Morphologically, in the lesions two principal types of yeast-like fungi may be distinguished (*a*) the *blastomycetoid* (*Blastomycetic*) type, (*b*) the *cryptococcoid* (*saccharomycetic*) type.

The characters of the blastomycetoid type are the following: Cells large, double contour very well marked, granules or spherules in the protoplasm very evident and of comparatively large dimensions. The characters of the cryptococcoid (or saccharomycetic) type, are the following: Cells generally smaller, double contour absent or much less marked, protoplasmatic granules not so evident and usually much finer.

These fungi belong to widely different botanical groups; when cultivated, some of them show the same morphological characters as in the lesions, viz., oval or roundish budding cells, with no

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mycelium, but quite a number of them show mycelium, and some, in fact, practically mycelium only.

Classification of yeast-like fungi (budding fungi). The late Dr. Chalmers and myself have given a botanical classification of these organisms in the third edition of our "Manual of Tropical Medicine." Some of them are Ascomycetes, others are Fungi Imperfecti; the principal families to which they belong are the following:

a. In cultures, budding cells, and in addition asci and ascospores present, no mycelium—Family Saccharomycetaceae, Rees, 1870.

b. Same as (*a*), but mycelium present—Family Endomycetaceae, Rees.

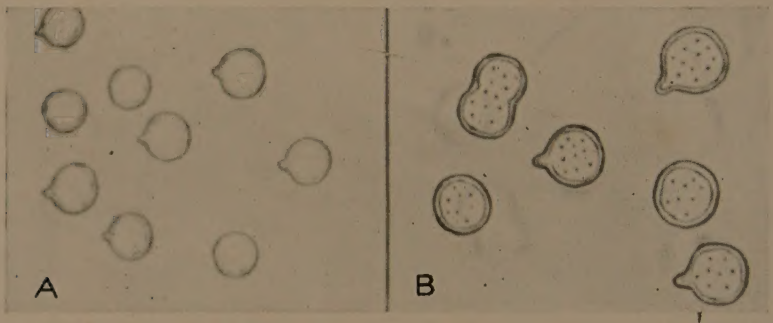


FIG. 1. YEAST-LIKE FUNGI. *A*, CRYPTOCOCCOID TYPE; *B*, BLASTOMYCOID TYPE

c. In cultures, budding cells (blastospores) present, no asci and no mycelium—Family Cryptococcaceae, Kützing, 1833.

d. Same as (*c*), but mycelium present,—Family Oosporaceae, Saccardo.

Each family contains a number of genera, a brief description of which may be found in Castellani and Chalmers' "Manual of Tropical Medicine," and also in the Gehrmann Lectures, University of Illinois, 1926 (Fungi and Fungous Diseases, by Aldo Castellani).

The following genera concern us—*Blastomycoides, Cryptococcus, Saccharomyces, Debaryomyces, Monilia, Willia.*

GENUS BLASTOMYCOIDES CASTELLANI, 1926

Synonyms. Blastomyces, Odium pro parte, Cryptococcus pro parte, Coccidioides pro parte, Zymonema pro parte.

Remarks. As unfortunately, for botanical reasons, the generic term *Blastomyces* can not stand, I suggested recently the creation of a new genus, *Blastomycoides*, which should be placed in the Family Oosporaceae rather than in the Family Cryptococcaceae.

Definition. The genus *Blastomycoides* may be defined as follows: "Oosporaceae, with abundant mycelium and aerial

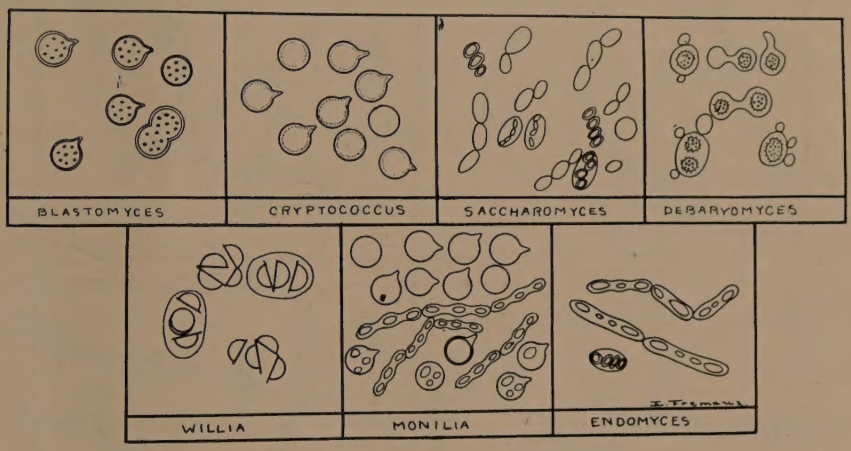


FIG. 2. PRINCIPAL TYPES OF YEAST-LIKE FUNGI

hyphae when grown on glucose agar; abundant mycelium with, at times, lateral conidia when grown in glucose broth hanging drops; no gas fermentation of any sugar. In the lesions, only roundish or oval large cells are seen, at times, budding, with well-defined double contour and well-marked granulations in the plasma present, without any mycelium." This genus, in all probability contains a number of species, but for the time being the following may be differentiated: *Blastomycoides dermatitidis, Blastomycoides immitis, Blastomycoides tulanensis.* For the practical differentiation of these 3 types I have found it useful to grow the fungi on mannitol agar (1 per cent) and on lactose agar

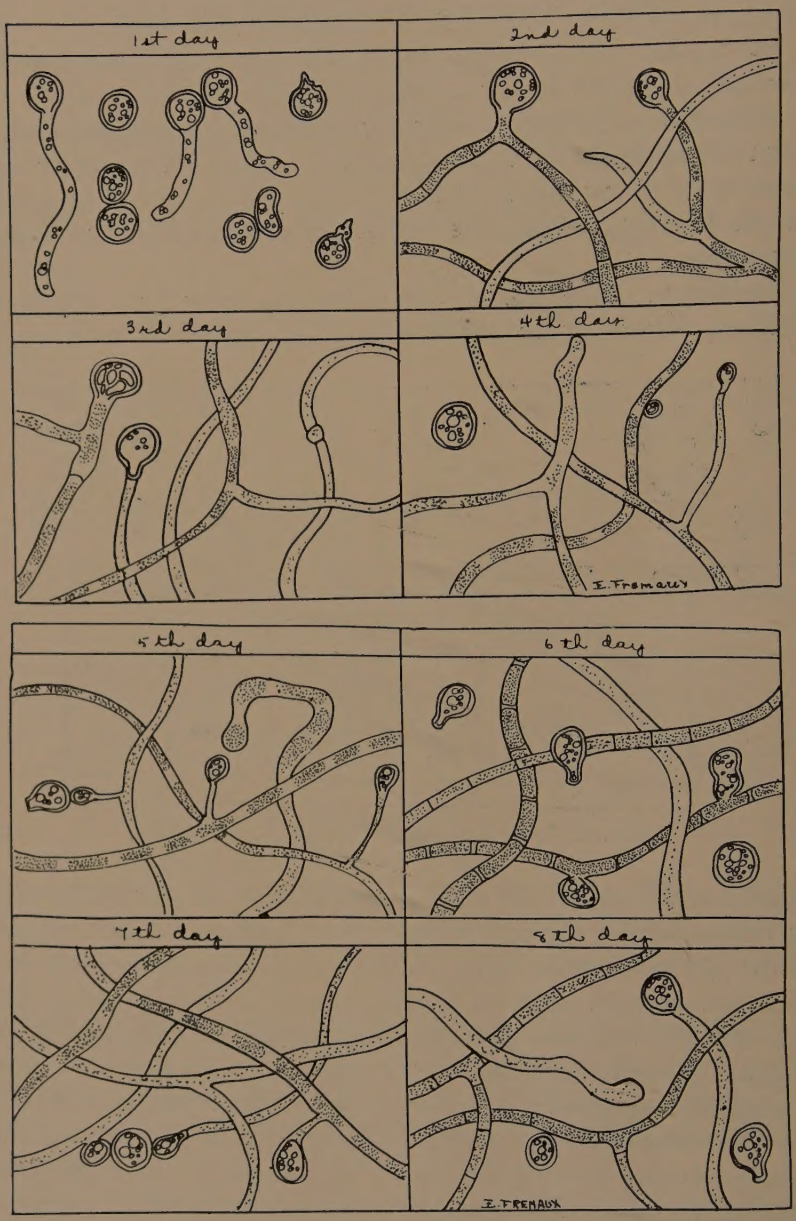


FIG. 3. BLASTOMYCOIDES IN CULTURE

(1 per cent), besides other media. The agar is made up with peptone water, not broth. Large tubes should be used, not the ordinary tubes used for bacterial cultures. The inoculated tubes are kept at 26°C. for two weeks and then examined. In a fairly warm climate like New Orleans keeping the tubes at the temperature of the room is satisfactory.

Blastomycoides dermatitidis Gilchrist and Stokes 1898 emen, Castellani. (*Synonyms: Blastomyces dermatitidis*, Gilchrist and Stokes, 1898; *Oidium dermatitidis* Ricketts; *Cryptococcus gilchristi* Vuillemin; *Zymonema gilchristi* de Beurmann and Gougerot, *Mycoderma gilchristi* Jannin 1913.

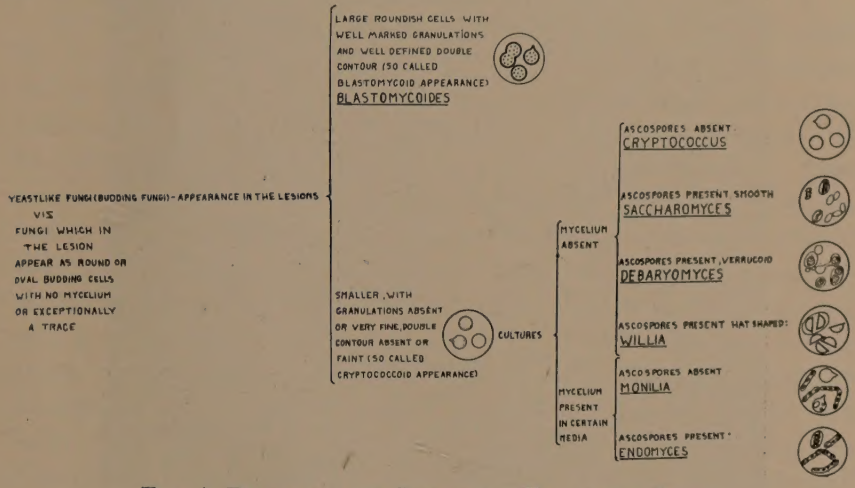


FIG. 4. DIAGRAMMATIC SCHEME OF YEASTLIKE FUNGI

In the lesions large roundish spore-like cells are found, 10 to 16 microns and much more, with a well-marked double contour and well-marked protoplasmatic granules. On glucose agar the growth is white or greyish and often fluffy; abundant mycelium is present; several tufts of longer aerial hyphae are often seen in the center. In mannitol agar (1 per cent) the growth is white-greyish with often a peculiar woolly surface. After a time (two to three weeks) there may be a darkening of the growth and of the medium. In glycerine agar (1 per cent) the growth is white,

fluffy. On potato the growth is abundant, with white duvet. In glucose broth and other sugar broths the growth takes place all over the medium, including the surface portion. In glucose

FIG. 5. *Blastomycoides dermatididis* GILCHRIST (HANGING DROP CULTURE)

broth and peptone water hanging drops made from glucose agar cultures, at times only mycelial threads are seen, with absence of, or only very scanty lateral conidia; if these are present they seem

to be mostly sessile. Certain strains however will produce fairly abundant conidia supported by sterigmata. Preparations from solid media cultures made from the deep parts, not from the fluffy portions, will show at times some large roundish cells very similar or identical to those found in the lesions. Gelatine is not liquefied. No gas fermentation of any sugar.

Blastomycoides immitis Rixford and Gilchrist 1897. *Synonyms. Coccidioides pyogenes* Rixford and Gilchrist 1896; *Oidium coccidioides* Ophüls 1905; *Oidium protozoides* Ophüls 1905; *Posadasia esferiformis* Canton, 1898; *Oidium immite* Verdun 1907; *Oidium pyogenes* Verdun 1906; *Mycoderma immitis* Brumpt 1925.

Remarks. For this fungus the genus *Coccidioides* was created by Rixford and Gilchrist in 1897. The principal characteristic would be the presence of very large asci with numerous ascospores. The botanical investigation I have carried out on two strains of this fungus did not show the presence of true ascospores. The numerous minute bodies described as ascospores inside the large round cells are not in my opinion ascospores; they are protoplasmatic granules or spherules. My contention seems to be proved by the fact that when one of the large roundish cells produces a bud which later becomes a mycelial filament the same minute bodies are seen in the bud and in the mycelium so produced. I venture to state therefore that for the present at least this fungus should not be considered to belong to the Ascomycetes but to the Fungi Imperfecti and being very similar to *Blastomycoides dermatitidis* should be placed in the same genus, viz., in the genus *Blastomycoides*.

Characters of the fungus in the lesions and in cultures. In the lesions large roundish or oval spore-like bodies are seen, 10 to 20 microns and even much larger. They have a well defined double contour and numerous minute roundish bodies are seen in the protoplasma which I am inclined to consider to be protoplasmatic granules or spherules. On mannitol agar 1 per cent after two weeks incubation at 26° but as a general rule also after the same period of incubation at 22° or at the room temperature the growth becomes of a black slate color and most of the me-

dium takes the same color. On glycerol agar the growth is white-greyish with a fluffy surface with a somewhat woolly appearance. On lactose agar the growth is whitish or greyish, there is no evident darkening of the medium. On potato it is usually white and fluffy. On carrot it is also white and fluffy. In glucose broth the fungus growth is both at the surface and bottom. In hanging drop cultures a large amount of mycelial threads are seen, lateral conidia supported by sterigmata are often absent or present only in small numbers. The mycelial threads seem to be of more slender dimensions than those of *B. dermatitidis* and certainly of those of *B. tulanensis*.

TABLE 1

Characters of the cultures after three weeks at 26°C.

	GLUCOSE AGAR	MANNITOL AGAR	LACTOSE AGAR	GALACTOSE AGAR
B. immitis	Whitish-greyish or light fawn	Growth and medium slate black color	White or greyish	Woolly, no pigmentation
B. dermatitidis	Whitish or greyish, fluffy	Frequently woolly appearance; often deep darkening of the growth and medium (black or slate black color)	Dark pigmentation; slate black with darkening of medium	Some dark pigmentation often develops
B. tulanensis	White, fluffy	Always white, no darkening of medium	White, medium not darkened	White, fluffy

BLASTOMYCOIDES TULANENSIS CASTELLANI, 1926

In the lesions large roundish or oval cells are found, 8 to 16 microns and even much larger with well-marked double contour and some granules or spherules in the protoplasma of fairly large size. On glucose agar the growth is white and somewhat fluffy, this being due to tufts of aerial hyphae. In mannitol agar the growth is white and the medium does not become darkened. On lactose agar the growth is white, there is no darkening of the

medium. In glycerol agar the growth is at times nodular with slight white duvet, at times fluffy white. In peptone water or glucose peptone water or glucose broth hanging drop cultures made from glucose agar cultures round lateral conidia sup-

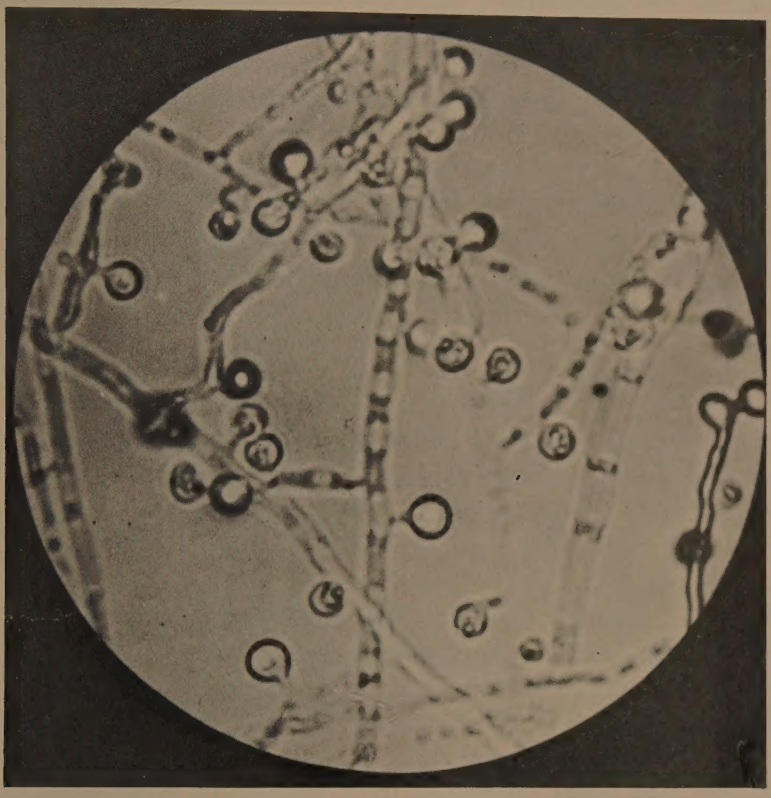


FIG. 6. *Blastomycoides tulanensis* (HANGING DROP CULTURE)

ported by well-developed sterigmata are usually present. In cultures on solid media especially in the submerged portion of the growth at times large round or oval cells with a well-marked double contour membrane and protoplasmatic granulations may be present very similar or identical to those found in the lesions.

Blastomycoides tulanensis on glucose agar and several other

media often grows like a trichophyton with white duvet and at times radiating furrows.

In table 1 are collected some differential cultural characters of the three types of *Blastomycoides*. On glucose agar the differences are slight or absent, but they are usually distinct on mannitol, lactose and glycerol agars. The tubes were kept at 26°C. for three weeks.

In practice the three types of *Blastomycoides* can be differentiated by using mannitol and lactose agar (1 per cent); *immitis* produces black pigmentation in mannitol but not in lactose, *dermatitidis* both in mannitol and lactose, *tulanensis* in neither mannitol nor lactose.

A fourth type or species of *Blastomycoides* may perhaps be accepted: this is a strain which gives black pigmentation in glucose agar and many other media (*B. niger*).

GENUS CRYPTOCOCCUS KÜTZING, 1833

Definition. Cryptococcaceae (budding fungi not forming ascospores) with vegetative elements not elongate; roundish or oval, with no very distinct double contour although there are exceptions; pathogenic and non-pathogenic; no globule of fat and only one bud at a time; and no formation of thick pellicle on fluid sugar media. Can be cultivated, the cultures consisting solely of roundish or oval cells with no mycelial filaments. Some species gas-ferment glucose and other sugars.

Principal species. For reasons already stated, and principally owing to the presence of a large amount of mycelium in cultures, the fungi described by Gilchrist in Blastomycosis—*Cryptococcus* (*Blastomyces*) *dermatitidis*—cannot be placed in this genus, as has often been done by some observers. The fungus found by Busse in a case of multiple abscesses and some fungi found by me in certain cases of blastomycosis of the tongue and in Blastomycosis furunculosa may be placed in this genus.

Cryptococcus hominis Vuillemin, 1901. Synonyms. Saccharomyces (sp.?) Busse, 1894; *Atelosaccharomyces busse-buschki* (Beurmann and Gougerot, 1909); *Atelosaccharomyces rudeli* of Beurmann and Gougerot, 1911.

This organism was found in multiple deep abscesses in a woman by Busse. In the pus the fungus was present in the shape of oval bodies, with a membrane which had a double contour. These elements were arranged in groups; each group was embedded in an amorphous substance and surrounded by a capsule. Culturally the fungus showed only roundish budding forms, no mycelium and no asci. Growth on solid mediums was generally white with at times a yellowish tinge. Gelatine was not liquefied.

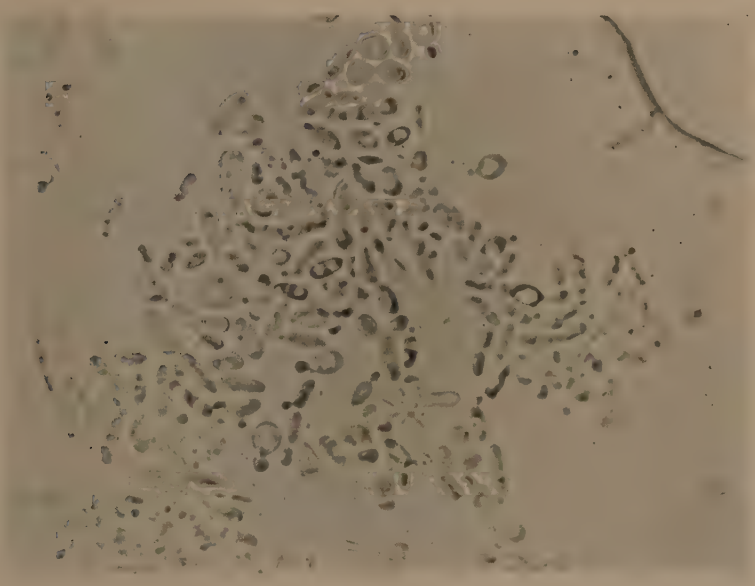


FIG. 7. *Cryptococcus macroglossiae*

According to Sasagawa, this fungus produces acidity in glucose, levulose, mannitol and galactose. The organism was pathogenic to rabbits, white mice and dogs.

Cryptococcus (Monilia) macroglossiae Castellani, 1925. In Ceylon during the period 1903–1915 I observed 3 cases of a peculiar type of macroglossia of blastomycetic origin. Two years ago an interesting case of macroglossia of the same type was referred to me in London by Dr. Broughton Alcock, and in this case, too, I isolated a yeast-like organism.

Description of the organism. It is a yeastlike fungus, Gram-positive and not acid-fast. The individual cells are oval and of rather large dimensions, the maximum diameter varying between 4 and 5 microns.

Cultural and biochemical characters. On dextrose agar there is abundant growth, white, with a smooth surface. On ordinary agar there are the same characters as on dextrose agar, but they are less abundant. Glycerin and serum are not liquefied.

Sugar peptone water. The organism does not produce gas in any sugar or other carbohydrate. Rarely it may produce a slight amount of acidity in dextrose.

Litmus milk. In litmus milk there is no change.

Agglutination. It is agglutinated by the patient's blood (1 in 400); not agglutinated, or only slightly so, by the blood of patients suffering from furunculosis blastomycetica.

Presence of asci and mycelium. Asci have never been observed even in very old cultures; a little mycelium is not rarely visible in certain cultures, especially in fluid mediums. It would, therefore, probably be more correct to place this fungus in the genus *Monilia*, instead of the genus *Cryptococcus*. If it is placed in the genus *Monilia* it belongs to the zeylanica type (absence of gas in every sugar); it differs from *Monilia zeylanica* in not producing pigment, the cultures of *Monilia zeylanica* being yellow. The correct name for the organism would be *Monilia macroglossiae* Castellani (synonym, *Cryptococcus macroglossiae* Castellani).

Remarks on macroglossia blastomycetica. The whole tongue is greatly enlarged, occasionally painful; the patient feels discomfort in eating and may have some difficulty in speaking; he cannot whistle. It may be difficult to make the clinical diagnosis of blastomycetic macroglossia, as the tongue, though greatly enlarged, may show almost complete absence of the verrucoid patches so typical of blastomycosis. Deep scrapings should be made from the tongue after it is dried and painted with tincture of iodine, and cultures should be made. The observation of yeast-like organisms in superficial scrapings of the tongue is without importance, as these fungi are not rarely found in that situation even in normal mouths. Potassium iodide has a beneficial effect on the condition. Vaccines prepared with the fungus seem to be useful.

Cryptococcus castellanii Re, 1925. Synonyms: *Monilia* (Sp.?) Castellani, 1924; *Monilia castellani* Re, 1925. Isolated by me from peculiar cases of persistent furunculosis, not answering to

staphylococcus vaccine (Blastomycosis furunculosa) Furunculosis blastomycetica).

Description (English cases). Morphologically the organism is yeast-like, Gram-positive and not acid-fast. The individual cells are some-

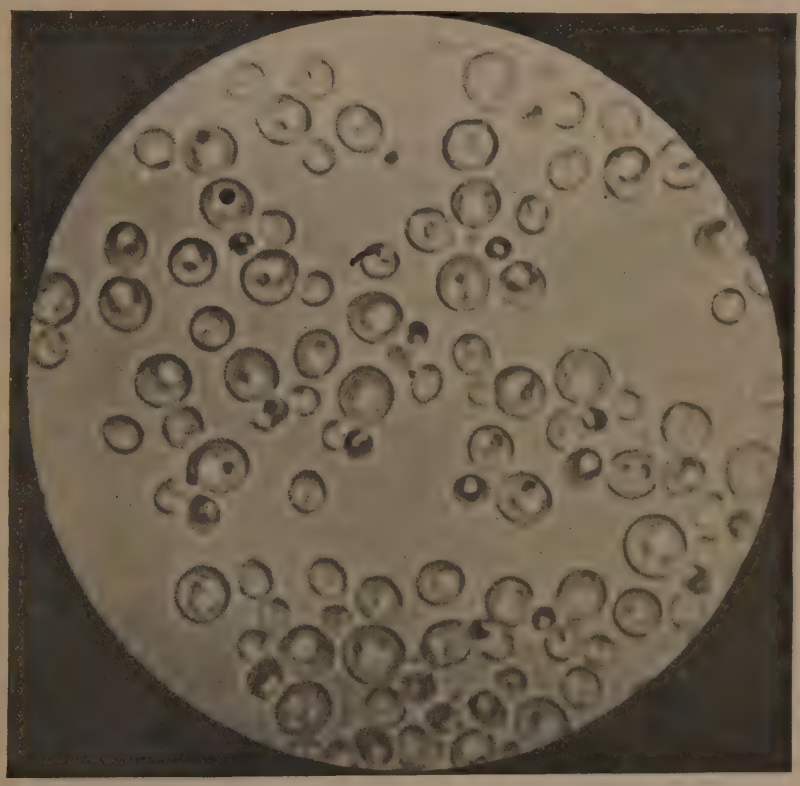


FIG. 8. *Cryptococcus castellanii* RE

what rounded or oval. The maximum diameter of most cells is from 3 to 4 microns. The fungus is seldom detected microscopically in the pus of the boil-like lesions, staphylococci generally being present in large numbers; cultural methods are necessary; the cultures from the pus, as a rule, resemble cultures of *Staphylococcus aureus*. It may be necessary to make a dozen or more preparations from what looks like a

pure staphylococcus growth to find a few yeast-like cells. By plating and replating on dextrose agar mediums the fungus is finally isolated.

Cultural and biochemical characters. The fungus grows abundantly on dextrose agar and grows also well, though less abundantly, on ordinary agar. The cultures on dextrose agar are at first white, but after a few days they show a characteristic yellowish or yellowish brownish pigmentation, with occasionally a purplish or reddish tinge. Gelatin and serum are not liquefied.

Lead agar is not darkened during the first two weeks; later a slight darkening may occasionally take place.

Sugar peptone waters. The fungus when recently isolated has little or no fermentative action on any sugar; it may produce a slight acidity in dextrose and levulose, and occasionally a slight amount of gas. When the fungus has been transplanted several times its fermentative action is greatly increased, and it generally produced acid and gas in dextrose and levulose and occasionally slight acidity in galactose; it does not form gas in any other sugars.

Litmus milk. The medium is not clotted; a slight acidity may be present.

Agglutination. The fungus is agglutinated by the patient's blood in certain cases up to 1 in 400.

Ascospores and mycelium. I have never found asci even in extremely old cultures, mycelium in small amount is not rarely present in certain mediums, especially fluid mediums. A more complete description may be found in the Journal of Tropical Medicine and Hygiene, June 15, 1925.

Cryptococcus farciminosus Rivolta and Miscellone, 1883. Synonyms. *Cryptococcus tokishigei* Vuillemin; *Lymphosporidium eqi* Gasperini, 1908; *Leukocytozoon piroplasmoides* Ducloux, 1908.

Definition. Vegetative cells in situ, oval or roundish, with well marked double contour.

Remarks. This organism is often included in hypertrophied endothelial cells and in leukocytes in the lesions in horses suffering from lymphangitis epizootica in Europe, Africa, Asia and America.

Cultivation. It is difficult to cultivate. Negre and Boquet have used with success a medium made of agar and dried horse dung. Sugar reactions are unknown.

Cryptococcus epidermidis Castellani, 1914. Found by me in saccharomycosis or cryptococcosis epidermica; cells of variable size; has not yet been cultivated.

Cryptococcus capsulatus Darling, 1906. Synonym. *Histoplasma capsulatum* Darling, 1906.

Definition. In the affected tissue the parasite appears in round or oval form, measuring from 1 to 4 microns in diameter and enclosed in an achromatic refractile capsule. Cultivation so far has been negative.

Remarks. This organism was found by Darling in the endothelial cells of capillaries and small blood vessels in the lungs, spleen, liver, intestines and lymph glands, as well as in the leukocytes. It was considered by Darling and others to be a protozoon, and for it the genus *Histoplasma* was created. At present there is a consensus of opinion that it is a *Cryptococococcus.*

Pathogenicity. This fungus is pathogenic for man, causing disseminated, hyaline, pseudogranulomas in the lungs, splenomegaly, necrotic areas in the liver and ulceration of the small and large intestines.

Cryptococcus histolyticus Stoddard and Cutler, 1916. Synonym. *Torula histolytica* Stoddard and Cutler. Found in a case of mycotic cerebrospinal meningitis (Freeman and Weidman); cultures yellowish. Produces acidity in glucose, maltose, saccharose and dextrine.

Cryptococcus ruber Demne, 1889. Synonym. *Saccharomyces ruber* Demne, 1889.

This organism was found in the stools of children suffering from enteritis and also in certain specimens of milk.

It grows easily on ordinary laboratory mediums, producing red colonies. According to Casagrandi, it does not ferment any sugar.

Cryptococcus pararoseus Castellani, 1926. Isolated by me from the sputum of patients in the tropics with chronic bronchitis. Grows well on all ordinary mediums. The growth has a smooth surface and is pink or pink-red. It produces slight acidity in glucose and levulose.

Cryptococcus metaniger Castellani, 1926. Isolated by me from a peculiar variety of *Trichomycosis nigra.* The cells are rather elongated, and it is possible that further investigation will show that the fungus does not belong to the genus *Cryptococcus.* On glucose agar it produces a jet black growth. It differs from *C. niger* Vuillemin in that the cells are more elongated and that the cultures are black in all the ordinary laboratory mediums. *C. niger* Vuillemin was originally found by Muffucci and Sirleo in 1895 from a pulmonary myxoma of a guinea-pig.

The cells *in situ* have a thick mucilaginous membrane. The growth was brown or black on potato, but white on most other mediums.

Cryptococcus graciloides Castellani, 1925. Isolated by me from cases of stomatitis cryptococcobacillaris in Central America. It is generally found living in symbiosis with *Bacillus vermiculoides* Castellani, 1925, from which it may be separated with difficulty.

This cryptococcus is a delicate yeastlike organism, Gram-positive and not acid-fast. Each cell is roundish or more often oval, with frequently a flasklike shape. In preparations from the cultures the average maximum longitudinal diameter of most cells is from 3 to 4.5 microns, and the maximum average transverse diameter is from 2 to 3 microns.

Cultural and biochemical characters. On dextrose agar, minute colonies somewhat streptococcus-like appear. On McConkey lactose agar there are minute colonies, but growth is often more abundant than on dextrose agar. In gelatin and serum growth is exceedingly scanty, and neither of the mediums is liquefied. With lead agar there is no evident darkening of the medium.

Sugar peptone waters. There is no fermentation of any sugar, but it must be noted that the fungus grows scantily in these mediums and that sometimes there is no growth.

There are many other species of less known cryptococci. The following may be mentioned, but none of these have been completely investigated biochemically.

Cryptococcus linguae-pilosae Lucet, 1901.
Cryptococcus plimmeri Constantin, 1901.
Cryptococcus degenerans Vuillemin, 1896.
Cryptococcus corsellii Neveu-Lemaire, 1908.
Cryptococcus breweri Verdun, 1912.
Cryptococcus tonkini Legendre, 1911.
Cryptococcus sulfureus Beauverie and Lesieur, 1912.
Cryptococcus lesieuri Beauverie and Lesieur, 1912.
Cryptococcus salmoneus Sartory, 1911.
Cryptococcus niger Vuillemin.
Cryptococcus guillermondi Beauverie and Lesieur, 1912.
Cryptococcus harteri Beurmann and Gougerot, 1913.
Cryptococcus hudelo Beurmann and Gougerot, 1914.
Cryptococcus membranogenes Steinhouse, 1916.

GENUS SACCHAROMYCES MEYEN, 1838

Definition. Saccharomycetaceae (viz. budding fungi producing ascospores) with smooth spores, spore membrane single; no evidence of any copulative process; occasionally rudimentary mycelial tubes present; with transverse septation; induce alcoholic fermentation.

Saccharomyces blanchardi Guiart, 1906. Found at an operation by Blanchard, Schwartz and J. Binot, on a patient who had been considered to be suffering from tubercular peritonitis. The fungus had produced in the peritoneum a large whitish, gelatiniform mass, weighing about 1 kgm. The fungus grew well on all sugar mediums.

On maltose agar it produced crateriform colonies of a snow-white color; asci with eight spores were present. On gelatin the growth was mucoid-like and gray. Liquefaction of the medium was slow. On potato there was a mucoid growth, whitish and darkening after a long time. On carrot the growth was viscid and abundant; it was pathogenic to rabbits, in which it induced a general mycosis, which terminated fatally.

Saccharomyces granulatus Vuillemin and Legrain, 1900. Observed by Vuillemin and Legrain in a tumor of the submaxillary bone; cells ovoid, from 4 to 5 microns in length, and from 3 to 4 microns in breadth; cultures pinkish or pinkish red; ascospores and chlamydospores present; gelatin not liquefied, sugar reactions not given.

Saccharomyces tumefaciens Curtis, 1896. *Synonym. Saccharomyces subcutaneus tumefaciens* Curtis, 1896. Found by Curtis in a myxomatous tumor. It appeared in the tissues in the shape of spherical bodies from 16 to 20 microns in diameter, each surrounded by a zone of amorphous substance; grows well on all sugar mediums; in old cultures asci are seen, with from one to four spores; gelatin with surface growth whitish, no liquefaction; said to ferment saccharose, but not maltose or lactose; action on dextrose not mentioned; pathogenic to rats and dogs.

Saccharomyces samboni Castellani, 1907. Cells roundish, from 4 to 8 microns in diameter, easily grown on various mediums, producing white colonies, which rapidly coalesce; found by me in

Ceylon in a few cases of intertriginous dermatitidis of the cruroscrotal region. A similar or identical organism has been observed by Whitfield in England in a case of the same dermatitidis. Ferments glucose, levulose and maltose; gelatin is not liquefied; in old cultures asci are occasionally present, but certain strains do not seem capable of producing asci and therefore probably belong to the genus *Cryptococcus*.

Saccharomyces hominis Klein and Gordon, 1903. Isolated in some cases of tonsillitis clinically resembling diphtheria; roundish or oval cells, from 5 to 7 microns in diameter; pathogenic to guinea-pigs and rabbits; sugar reactions unknown.

Saccharomyces anginae Achalme and Troisier, 1895. Found by Achalme and Troisier in a case of tonsillitis showing white patches; *in situ* cells ovoid, from 8 to 15 to 5 to 6 microns; in cultures 4 spores asci are present; on gelatin, surface growth white; ferments saccharose, but other reactions are not given.

Saccharomyces balzeri Balzer, Burnier and Gougerot, 1911. *Synonym. Parendomyces balzeri* Balzer, Burnier and Gougerot, 1911. Grows on culture mediums under the type of oval or roundish, yeast-like cells, proliferating by budding; isolated by Balzer, Burnier and Gougerot from a gummatous condition; sugar reactions unknown.

Saccharomyces cerevisiae Meyen; emendavit Hansen. *Synonym. Cryptococcus fermentum* Kützing; *Torula cerevisiae* Turpin; *Hormiscum cerevisiae* Bail.

Cells oval or roundish, ascospores formed at all temperatures between 12 and 37°C., optimum from 25 to 30°C.; abundant growth on all ordinary laboratory mediums; colonies, white, surface usually smooth. There are several varieties of *S. cerevisiae*. The one in my collection gas ferments dextrose, levulose, maltose, galactose and saccharose. This fungus and its varieties are used in the production of beer.

Saccharomyces ellipsoideus Hansen. Vegetative cells, mostly elliptical; optimum temperature for appearance of ascospores 25°C., but ascospore formation takes place at any temperature between 10 and 32°C. The ascus cell is of small dimensions, is ellipsoidal and contains from one to four ascospores which measure from 2 to 5 microns; according to Marchand, they germinate after having copulated two by

two. This *Saccharomyces* which is found on the surface of grapes plays an important rôle in the process of vinification.

Saccharomyces pastorianus Hansen. Vegetative cells roundish or oval, at times elongated; asci elongated, usually containing from 1 to 4 ascospores, each ascospore varies in size between 1.5 and 3.5 microns; occasionally much larger ascospores may be seen, up to 5 microns in diameter; optimum temperature for development of ascopores 27.5°C., but ascospore formation takes place at any temperature between 4 and 30.5°C.; at 31.5°C. formation of ascospores ceases completely. This fungus gives a bitter taste and a bad odor to beer.

GENUS DEBARYOMYCES KLOCHER

Definition. *Saccharomycetaceae* with ascospores presenting a verrucose surface. Several yeast-like organisms, some of which are found in scrapings from the skin and are probably non-pathogenic, have been classified in this genus by Ota. A pathogenic one is *Debaryomyces hudeloi* (de Berumann and Gourgerot, 1909), Fonseca emendavit 1922. Asci, which are scanty, contain one spore with a verrucose surface. The fungus is said to ferment glucose and saccharose, but not levulose, maltose, galactose or lactose. It was found by Hudelo, Rubens, Duval and Laederich in a case of multiple abscess in France (Busse-Buschke type of blastomycosis). The vegetative cells are roundish or oval, occasionally elongated. They are from 2 to 4 microns, in diameter, and when elongated from 6 to 8 microns.

GENUS WILLIA HANSEN, 1904

Definition. *Saccharomycetaceae* with ascospores lemon-shaped or hat-shaped; as a rule they do not produce alcoholic fermentation, but do produce various ethers; cultures present a pleasant fruity odor.

Species in man. *Willia anomala* Hansen, 1904.

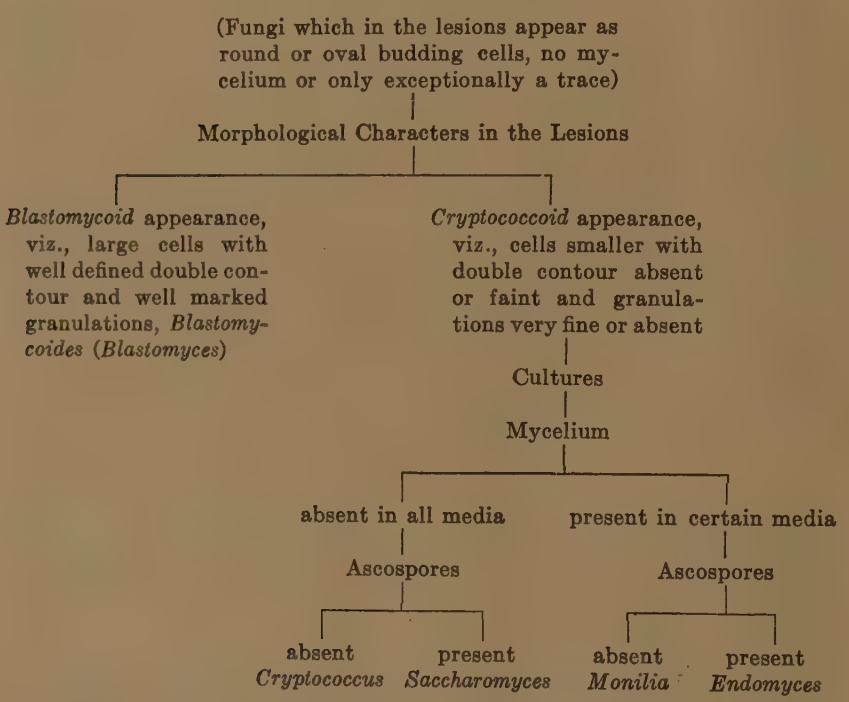
Willia anomala Hansen, 1904. Rather small oval cells; in sugar liquid mediums it forms a well marked membrane, containing air bubbles; asci with from two to four spores of the so-called hat-like type; dextrose fermented, but not saccharose or maltose; ferments beer-wort, with production of ethers; found by Beauverie and Lessieur in the sputum of a tuberculous patient.

A fungus which probably belongs to the genus Willia was found by me in scrapings from the inguinal region of a man.

GENUS MONILIA PERSOON, 1797

As regards the botanical characters of the genus *Monilia*, the original definition by Persoon is *Stipitata aut effusa byssoidea, Fila moniliformis articulata.* These fungi are stated to be characterized by the sporophores being simple or subsimple, and producing by constriction at their extremities, a chain of large,

Key to the principal groups of yeast-like fungi (budding fungi)



lemon-shaped conidia, often provided with a disjunction apparatus. The general tendency at the present time, however, is to extend the term "*Monilia*" so as to include all those organisms of the family Oosporaceae Saccardo, 1886, the vegetative body

of which (thallus) in its parasitic life (*in situ* in the lesions) appears composed of mycelial threads and free budding forms, some of the mycelial filaments being long and branched, and of rather a large size, and often presenting arthrospores. In the saprophytic life (cultures on the usual solid laboratory media) mostly yeast-like, roundish or oval bodies are seen, while mycelial filaments are very scarce or absent, and when present they are rather short and consist only of a few articles. Some monilias show very little mycelium also in the lesions. Monilia fungi very often ferment glucose and other carbohydrates with the production of gas.

Classification. Morphologically, monilias may be separated into two groups: (1) the free budding cells are roundish, and (2) the free budding cells are oval or elongated. Morphological characters, however, will not help further in the classification of these fungi, and for some years I have recommended a biochemical classification. For practical purposes monilias may be conveniently classified according to some of their biochemical characters, as follows:

1. Gas produced in dextrose only. *Balcanica group.* Principal species: *Monilia balcanica,* Castellani; *Monilia parabalcanica,* Castellani.

2. Gas produced in dextrose and levulose. *Krusei group.* Principal species: *Monilia krusei,* Castellani; *Monilia parakrusei, Monilia castellanii* Re, probably a cryptococcus. Of *Monilia krusei* there seem to be two morphological varieties: one oval, the original Krusei, the other showing the same biochemical characters but of a roundish shape.

3. Gas produced in dextrose, levulose and maltose. *Pinoyi group.* Principal species: *Monilia pinoyi* Castellani; *Monilia nabarroi* Castellani.

4. Gas produced in dextrose, levulose, maltose and galactose. *Metalondinensis group.* Principal species: *Monilia metalondinensis* Castellani; *Monilia pseudometalondinensis* Castellani.

5. Gas produced in dextrose, levulose, maltose, galactose, and saccharose. *Tropicalis group.* Principal species: *Monilia tropicalis* Castellani; *Monilia metatropicalis* Castellani.

TABLE 2

Biochemical characters of certain Monilias

	GLUCOSE	LEVULOSE	MALTOSE	GALACTOSE	RHAMNOSE	LACTOSE	MANNITOL	DULCITOL	DEXTRIN	RAFFINOSE	ARABINOSE	ADONITOL	INULIN	SORBITOL	STARCH	GLYCERINE	INOSITOL	SALICIN	AMYGDALIN	ISODULCITOL	ERYTHRITE	GELATINE	SERUM	LITMUS MILK		REMARKS
Monilia zeylanica Castellani	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	C	Yellowish	
Monilia zeylanoides Castellani	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	White	Produces no discoloration of lead agar
Monilia (cryptococcus) macroglossiae Castellani	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	White	Produces black discoloration of lead agar
Monilia balcanica Castellani	G	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	White	
Monilia parabalcanica Castellani	G	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	C	White	
Monilia krusei Castellani	G	G	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	White	
Monilia parakrusei Castellani	G	G	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	C	White	
Monilia (cryptococcus) castellanii Re.	G	G	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	Yellowish or reddish-brownish	This fungus is probably a true cryptococcus. The peculiar reddish-brownish color is best seen in old potato cultures
Monilia pinoyi Castellani	G	G	G	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	White	
Monilia nabarroi Castellani	G	G	G	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	C	White	
Monilia metalondinensis Castellani	G	G	G	G	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	White	
Monilia pseudolondinensis Castellani	G	G	G	G	0	0	0	0	G	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	White	
Monilia alba Castellani	G	G	G	G	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	C	White	
Monilia pseudolondinoides Castellani	G	G	G	G	0	0	0	0	G	0	0	0	0	0	0	0	0	0	0	0	0	0	0	C	White	
Monilia africana Macfie, 1921	G	G	G	0	G	0	0	0	G	G	0	—	0	0	0	0	0	0	0	0	0	0	0	0	White	

Monilia albicans Robin, emend, Castellani and Chalmers	G	G	G	G	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	+	+	0	White
Monilia tropicalis Castellani	G	G	G	G	G	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	White
Monilia metatropicalis Castellani	G	G	G	G	G	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	C	White
Monilia rhoi Castellani	G	G	0	G	G	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	White
Monilia guillermondi Castellani	G	G	0	0	G	0	0	0	0	G	0	0	0	0	0	0	0	0	0	0	0	0	0	White
Monilia pseudoguillermondi Castellani	G	G	0	0	G	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	C or P	White
Monilia macedoniensis Castellani	G	G	0	G	G	0	0	0	0	0	0	0	G	0	0	0	0	0	0	0	0	0	C	White
Monilia macedoniensoides Castellani	G	G	0	G	G	0	0	0	0	0	0	0	G	0	0	0	0	0	0	0	0	0	0	White
Monilia chalmersi Castellani	G	G	0	G	G	0	0	0	0	0	0	0	G	0	0	0	0	0	0	0	0	0	0	Dark brown
Monilia parachalmersi Castellani	G	G	0	G	G	0	0	0	0	0	0	0	G	0	0	0	0	0	0	0	+	0	C	White
Monilia bronchialis Castellani	G	G	G	0	G	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	White
Monilia pseudotropicalis I	G	G	0	G	G	G	0	0	0	0	G	0	0	0	0	0	0	0	0	0	0	0	C	White
Monilia pseudotropicalis II	G	G	0	G	G	G	0	0	0	0	0	0	G	0	0	0	0	0	0	0	0	0	0	White
Monilia pseudotropicalis III	G	G	0	G	G	G	0	0	0	0	0	0	G	0	0	0	0	0	0	0	0	0	C	White
Monilia pseudotropicalis IV	G	G	0	G	G	G	0	0	0	G	0	0	G	0	0	0	0	0	0	0	0	0	0	White

Note: G = production of gas; C = production of clot; 0 = negative result; — = gas absent, no clotting.

6. Gas produced in dextrose, levulose, galactose and saccharose. *Rhoi group.* Principal species: *Monilia rhoi* Castellani.

7. Gas produced in dextrose, levulose, maltose and saccharose. *Bronchialis group.* Principal species: *Monilia bronchialis.*

8. Gas produced in dextrose, levulose, saccharose and raffinose. *Guillermondi group.* Principal species: *Monilia guillermondi* Castellani; *Monilia pseudoguillermondi* Castellani.

9. Gas produced in dextrose, levulose, galactose, saccharose and inulin. *Macedoniensis group.* Principal species: *Monilia macedoniensis* Castellani; *Monilia macedoniensoides* Castellani; *Monilia chalmersi* Castellani.

10. Gas produced in lactose and other carbohydrates. *Pseudotropicalis group.* Principal species: *Monilia pseudotropicalis* Castellani, of which there are several varieties.

11. Gas produced in dextrin, in addition to other carbohydrates, but not in lactose. *Pseudolondinensis group.* Principal species: *Monilia pseudolondinensis* Castellani; *Monilia pseudolondinoides* Castellani; *Monilia africana* Macfie.

12. No gas produced in any sugar. *Zeylanica group.* Principal species: *Monilia zeylanica* Castellani; *Monilia zeylanoides* Castellani; *Monilia macroglossiae* Castellani.

It is important to note that many monilias after a few transplantations lose some of their fermentative characters or these are altered. Hence, the determination of species is possible only when recently isolated strains are used. There are however, certain monilias, as, for instance, *M. krusei*, *M. metalondinensis*, *M. tropicalis* and *M. macedoniensis*, which possess permanent biochemical characters.

Further details on classification of the various species of the genus Monilia may be found in the Manual of Tropical Medicine (Castellani and Chalmers, footnote 3, p. 1081).

Pathogenicity and virulence. The subcutaneous, intravenous or intrapulmonary inoculation of some monilias into rabbits does not produce any symptoms; other monilias are virulent and cause the death of the rabbit. It is interesting to note that monilias with identical biochemical reactions may vary enormously in their virulence: some strains may be quite avirulent, while others are exceedingly virulent. (See table 2.)

Simple classification of yeast-like fungi (budding fungi) for the use of the clinician and clinical pathologist. An elaborate botanical classification is not necessary for the purposes of the clinician and clinical pathologist, and the simple scheme shown in the tables may be of practical use to them.

CLASSIFICATION OF SKIN DISEASES DUE TO YEAST-LIKE FUNGI

The principal dermatomycoses due to "yeast-like fungi" (or budding fungi) may be classified as follows:

A. Mycotic infection deep:

1. Blastomycosis, Gilchrist type (*Blastomycosis verrucosa*).
2. Blastomycosis, Wernike type (*Blastomycosis ulcerativa profunda*) seu mutilans.
3. Blastomycosis, Kartulis type (*Blastomycosis glutealis*).
4. Blastomycosis, Busse type (*Blastomycosis purulenta profunda*).
5. Blastomycosis furunculosa (*Furunculosis cryptococcica*) (including paronychia blastomycetica, vel moniliaca, vel cryptococcica).
6. Pyosis blastomycetica.

B. Mycotic infection superficial:

1. Intertrigo blastomycetica, vel moniliaca, vel cryptococcica vel saccharomycetica.
2. Cryptococcosis epidermica.
3. Prickly heat according to certain authorities.

At the present time the tendency everywhere is to limit the term "Blastomycosis" to the conditions of Group A, and in this country to limit it to only the first four conditions of Group A.

(*1*) *Blastomycosis verrucosa*

(Synonym: Blastomycosis, Gilchrist type)

Clinical symptoms. This type is characterized by raised, roundish or oval patches with a verrucoid papillomatous or framboesiform surface, somewhat similar to tuberculosis verrucosa cutis, and in certain cases framboesia. The patches are not rarely surrounded by a violaceous halo. The following subtypes may be differentiated:

1. Affecting usually the skin only, but may, in addition, in a later stage affect the mucosae and internal organs; found all over the world, but principally in tropical and sub-tropical countries—Gilchrist type, *sensu stricto*.

2. Affecting solely or principally the oral or nasal mucosa; this type is especially common in South America. It is known also as South American oral blastomycosis or blastomycosis Lutz-Splendore type, and a description of it may be found in Castellani and Chalmers' "Manual of Tropical Medicine," third edition, p. 2084.

3. Affecting the tongue, causing at times an enormous increase in the size of this organ (macroglossia blastomycetica).

4. Affecting first the skin and later the internal organs, with symptoms of general infection and pyaemia (systemic blastomycosis).

To the above four subtypes a fifth one may be added to include a group of atypical cases in which the granulomatous framboesiform pustules are practically absent and only gumma-like swellings and sinuses are present.

Etiology. The fungi found are yeast-like fungi of the *Blastomyces* type (genus *Blastomycoides*, p. 2).

Diagnosis. In many cases the diagnosis can be made on clinical groups, but it should of course always be confirmed by mycological methods.

Treatment. If the diagnosis is made at an early stage potassium iodide may at times induce a cure provided it is given in massive doses and for long periods of time.

Prognosis. This is serious; if the diagnosis is made at an early stage and an appropriate treatment given, a complete cure may be obtained.

Illustrative cases

I will briefly quote 10 cases among those I have had the opportunity of investigating.

Case 1. Mr. M. while in Egypt during the Great War, noticed a papule near the left angle of the mouth, which later became moist and was covered by a small yellow crust. Other papules appeared and a

patch formed. He reported to the medical officer who suggested syphilis. The Wassermann reaction was negative; he had, however, a course of neosalvarsan without any benefit. During this treatment the condition spread to the mucosa of the lips and later to the tongue. After leaving the Army he consulted various medical men, some of whom

FIG. 9. BLASTOMYCOSIS (DR. HOPKIN'S CASE)

suspected syphilis, others a tuberculide. Finally, in 1920, he went to see Sir James Cantlie, who kindly referred him to me. I suspected blastomycosis, and succeeded in growing a fungus, which recent investigation has shown to be very similar to *Blastomyces tulanensis*. After several relapses he apparently recovered completely after a treatment of potassium iodide in large doses, and vaccine.

Case 2. (Blastomycosis of the nose.) Mr. T., of Bradford, consulted me in January, 1921; he had a rather large papillomatous mass on the left ala of the nose, with severe loss of substance. The condition

Fig. 10. Blastomycosis of the Lungs (Dr. Hopkin's Case)

had started during the war while the patient was in the Balkans, and had been considered a syphilide or a tuberculide. He had been treated with salvarsan, mercurial preparations and x-rays. I grew a fungus with characters somewhat similar to blastomycosis dermatitidis; in addi-

tion, a monilia-like fungus was grown with all the biochemical characters of *Monilia metalondinensis*. The condition yielded to potassium iodide in massive doses, but it took more than a year for a complete cure to be achieved.

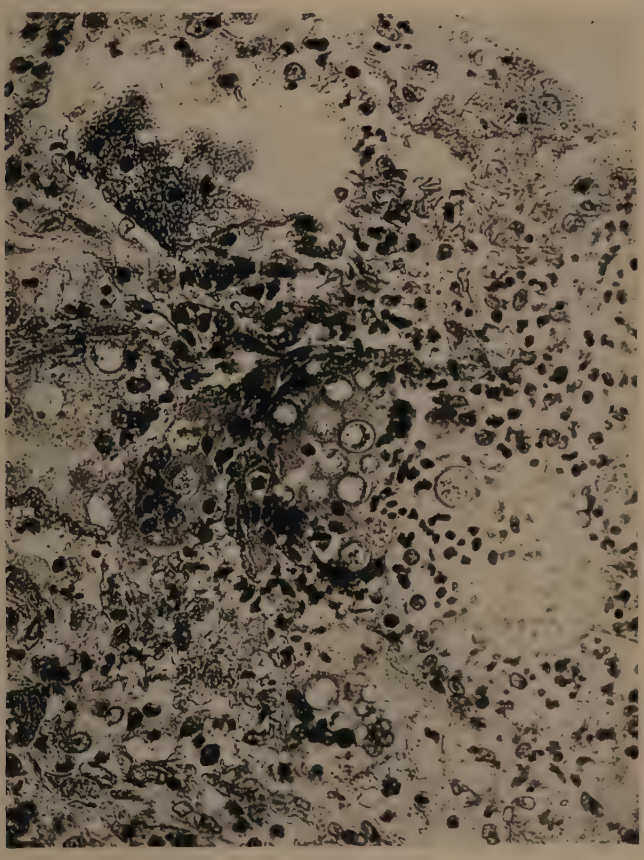


FIG. 11. BLASTOMYCOSIS OF LUNG (CASE OF DRS. DUVAL AND HARRIS)

Case 3. (Mild type of oral blastomycosis.) Master N. four years ago showed white patches on the tonsils and oral mucosa, apparently very similar to patches of thrush. Later several flattened nodules developed on the mucosa of the lower lip with a papillomatous surface. For these patches various diagnoses were suggested and various treatments were carried out without any benefit. He consulted me two years

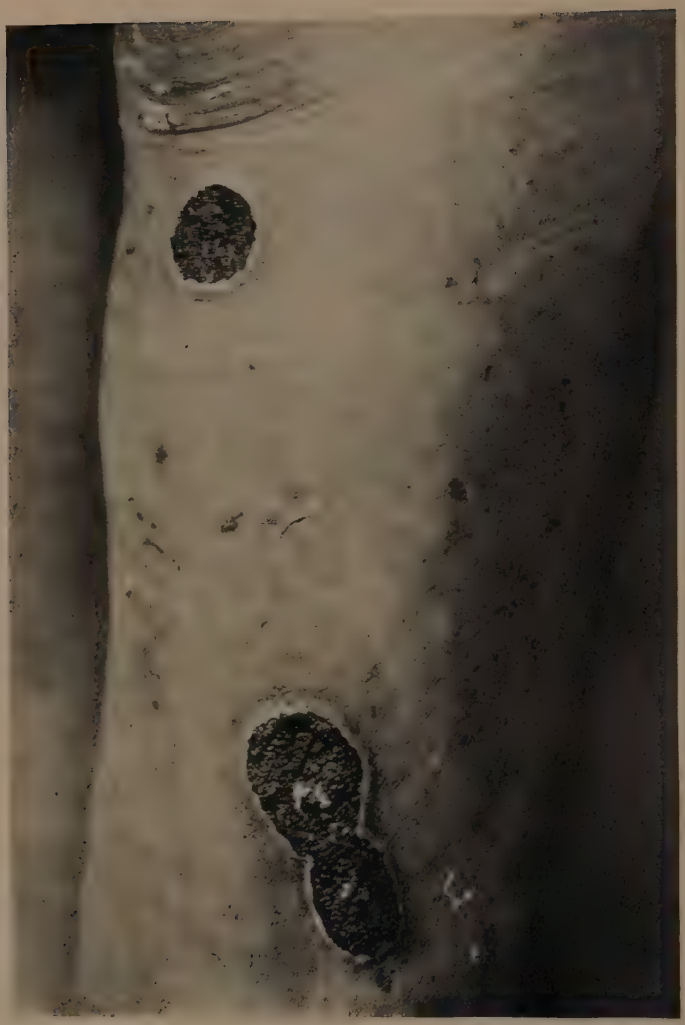


FIG. 12. BLASTOMYCOSIS (CASE FROM WHICH *B. tulanensis* WAS ISOLATED)

ago. The surface of one of the patches was scraped and from the deep parts of the lesion a fungus was found with the characters of a monilia, biochemically similar to *Monilia metalondinesis.*

The characters of the fungus are briefly the following: In the lesions only roundish budding cells are seen; in cultures a slight amount of my-

celium is present. Milk not clotted. Gas produced in glucose, levulose, maltose and galactose.

Case 4. (Blastomycosis of the tongue) *Macroglossia blastomycetica.* In Ceylon, during the period 1903–1915, I observed 3 cases of a peculiar

Fig. 13. Blastomycosis of Face

type of macroglossia of blastomycotic origin. Four years ago an interesting case of the same type was kindly sent to me by my friend, Dr. Broughton Alcock. The tongue was enormously enlarged and occasionally painful; the patient felt discomfort in eating and difficulty in speaking; he could not whistle; the surface of the tongue was somewhat roughened in places, but no very typical verrucoid patches were present.

Deep scrapings were made from the tongue, after drying and painting with tincture of iodine, and cultures were made. A fungus was grown,

Fig. 14. Blastomycosis of the Tongue

which I at first placed in the genus *Cryptococcus*, and later in the genus Monilia; *Monilia macroglossiae*. (For description of the fungus see

page 7.) A prolonged treatment with potassium iodide in very large doses and fungus vaccine induced an apparent cure.

FIG. 15. BLASTOMYCOSIS (IMMITIS TYPE)

Case 5. Mr. N., a white workman in New Orleans, two years ago developed verrucose patches on the hands and forearms and on the face. A fungus was grown with the characters of *Blastomycoides dermatitidis.*

Case 6. Mr. R., New Orleans. Typical patches on the face and arms. I was asked by Dr. Hopkins to investigate the case. A fungus was grown with the characters of *Blastomycoides tulanensis.*

Case 7. Negro, New Orleans. Framboesiform lesions on face. I was asked by Dr. van Studdiford to investigate the case mycologically.

Case 8. Mrs. B., New Orleans. Large verrucoid patches on the right forearm. A fungus was isolated with the characters of *Blastomycoides tulanensis.*

Case 9. Mr. O. P., New Orleans. Typical verrucoid patches on the face. A fungus was isolated with the characters of *Blastomycoides tualensis.*

Case 10. Young negro girl. Articular and periarticular lesions, gumma-like swelling and sinuses closely simulating tuberculosis. After a time she developed signs of broncho-alveolitis and of meningitis. At the post-mortem the lungs and all internal organs were found studded with white nodules of blastomycetic origin. *B. tulanensis* was isolated.

(*2*) *Blastomycosis ulcerativa profunda seu mutilanes*

(Wernicke type, Californian type, Coccidiodes type)

In most cases verrucoid lesions are present but in addition large deep ulcerative processes develop, the course being progressive and no treatment being of any avail. This type has been reported from South America and California and is due to *B. immitis.*

(*3*) *Blastomycosis purulenta profunda*

(Blastomycosis, Busse type; Blastomycosis subcutanea purulenta)

This type of blastomycosis is considered a variety of blastomycosis cutis for convenience sake. It is characterized by the presence of subcutaneous and deep abscesses, and purulent conditions of the bones, periosteum, and internal organs. The skin proper is not usually affected, and the verrucoid framboesiform patches are absent.

Etiology. The condition is caused by *Cryptococcus hominis*

Vuillemin, 1901, a term which probably covers several varieties or even species.

Cryptococcus hominis Vuillemin, 1901. (*Synonyms: Saccharomyces* (sp.?) Busse, 1894; *Atelosaccharomyces bussebuschki* de Beurmann and Gougerot, 1909; *Atelosaccharomyces rudeli* de Beurmann and Gougerot, 1911).

Found by Busse in abscesses in a woman. In the pus the fungus presented itself in the shape of oval bodies, with a membrane having a double contour. These elements were arranged in groups, each group embedded in amorphous substance and surrounded by a capsule. Culturally the fungus showed only roundish budding forms, no mycelium, no asci. Growth on solid media generally white. Gelatin not liquefied. Glucose fermented. Pathogenic to rabbits, white mice and dogs.

(4) *Blastomycosis glutealis*

This condition was described by Kartulis some years ago in Egypt. I have often observed it in Ceylon. The skin of the gluteal region—one nate or both nates—presents a diffuse induration, and is cribrated with the opening of sinuses, from which a thin pus exudes. The sinuses may be very deep and connected with each other, but in cases I have seen did not connect with the intestine. The pus does not contain grains, as is the case with actinomycosis. The patient may complain of pain and discomfort on sitting down. The disease is chronic.

Etiology. The cytological investigation of the condition cannot be considered completed. The fungi found seem to belong to the genus *Monilia* and the genus *Cryptococcus*. One of them has been imperfectly described as *C. kartulisi*.

(5) *Blastomycosis furunculosa*

Synonyms. Folliculitis decalvans cryptococcica, pro parte, furunculosis cryptococcica; pseudofurunculosis blastomycetica; furunculosis moniliaca; furunculosis mycetica; folliculitis decalvans saccharomycetica; folliculitis decalvans moniliaca.

History. Some years ago I described a peculiar type of blastomycosis indistinguishable clinically from ordinary furunculosis,

which I called at the time "furunculosis cryptococcica," and as the condition in the first 2 cases affected principally the scalp under the form of a purulent folliculitis and loss of hair, I also suggested for it the term "folliculitis decalvans cryptococcica." To date I have seen 5 cases; three patients contracted the infection in Great Britain, and two in India.

FIG. 16. *Blastomycosis glutealis*

Etiology. The fungi found are yeast-like, and it is difficult to decide whether they belong to the genus *Cryptococcus* or to the genus *Monilia.* One of them (*Cryptococcus castellanii* Re) was fairly completely described by me, and later by Dr. Re, who named it *Cryptococcus castellanii.* The strains of fungus isolated from the Indian cases are somewhat different from the organisms grown from the English cases, and differ also, though slightly, among themselves.

Symptomatology. The clinical picture of this blastomycosis is totally different from the usual types of blastomycosis cutis, which are characterized by the presence of patches with vegetating capillary excrescences which give them a characteristic verrucose or warty appearance.

Furunculosis blastomycetica is clinically indistinguishable from ordinary severe furunculosis. Boils, indistinguishable from ordinary boils, may be present on the face and body, but the region mostly affected, as a rule, is the scalp. In this region numerous pustules, flattened or conical, each pierced by a hair, may be seen; in addition, there may be infiltrated lesions which somewhat resemble flat carbuncles, and later open and discharge through several openings.

The hair in the infected areas falls off, and patches of baldness, sometimes permanent, remain.

Illustrative case

Mr. D., married, aged thirty-four, a Dane who had resided in London for twelve years preceding admission; he was fond of all outdoor sport, and was a famous football player. The condition started in March, 1921, with apparently follicular pustules on the scalp, and two or three furuncular-like lesions on the forehead and face. Later, extremely painful carbuncle-like lesions developed. A bacteriologic examination of the pus was made at a well-known clinical laboratory in London, and *Staphylococcus aureus* was found. An autogenous staphylococcus vaccine and also a stock vaccine were given for eighteen months without any benefit. On the advice of his medical attendant the patient then came to consult me.

Apart from the boil on the left forearm and one on the supraorbital region, all the lesions were on the scalp; several patches of baldness, with the skin smooth and whitish, were plainly visible; there were also numerous follicular pustules, some flat, some conical, and most of them surrounded by a zone of hyperemia. Two extremely painful carbuncle-like lesions, one not yet opened and the other with several openings discharging, were present. I made a bacteriologic and a mycologic examination. Microscopically, the pus contained only Gram-positive cocci. The dextrose-agar tubes inoculated with the pus showed abundant growth of *Staphylococcus aureus*. The microscopic examination of the

growth, however, showed here and there a yeast-like cell in several tubes. After plating and replating, this yeast-like organism was isolated with great difficulty. Later, I grew the same fungus from a number of lesions, some of which were unopened.

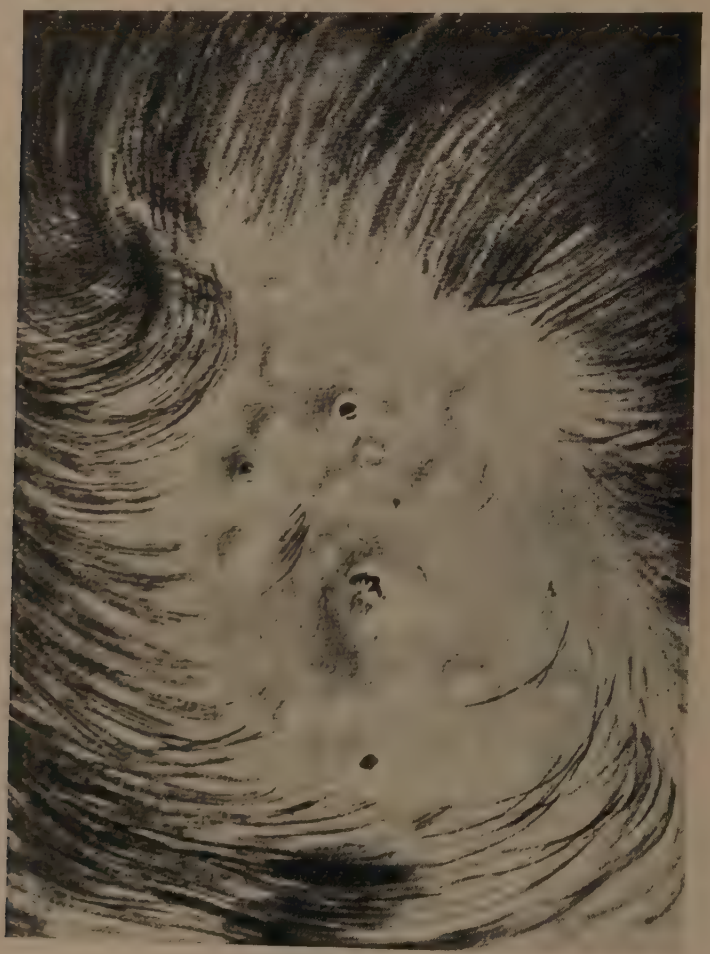


FIG. 17. *Blastomycosis furunculosa*

It was a cryptococcus with the following principal characters: Cultures on dextrose agar were abundant with a smooth surface, at first white and later yellowish. The fungus did not produce gas in any car-

bohydrate at first; later, it caused production of gas in dextrose and levulose. It was agglutinated by the patient's blood in his dilution

FIG. 18. *Blastomycosis furunculosa* (BALD PATCHES)

(1:400). An interesting point arises: Which organism was the true causative agent of the condition, the cryptococcus or the staphylococcus?

In my opinion, it was the cryptococcus, for the following reasons: Staphylococcus vaccines did not have any beneficial action whatever. The cryptococcus was agglutinated by the patient's blood, and the condition improved and finally disappeared under a treatment consisting of massive doses of potassium iodide given internally, and a cryptococcus vaccine subcutaneously injected. It is well known that potassium iodide does not have any beneficial action on *Staphylococcus furunculosis*, it makes it much worse.

Diagnosis. The diagnosis can be made only by mycologic method. In all cases of persistent furunculosis that do not answer to staphylococcus vaccine, the possibility of furunculosis blastomycetica should be kept in mind.

Prognosis. The disease does not have a tendency to spontaneous cure.

Treatment. Potassium iodide in large doses, given for long periods, often induces a cure. A vaccine prepared with the fungus seems to be useful, but used alone is not sufficient to bring about a cure.

Perionychia cryptococcica vel moniliaca

Synonyms. Perionychia saccharomycetica, perionychia mycetica, perionychia blastomycetica.

In patients suffering from Blastomycosis furunculosa a painful type of perionychia may develop associated with the presence of budding fungi usually of the genera *Monilia* and *Cryptococcus*, occasionally of the genera *Saccharomyces* and *Debaryomyces*. At times the lesions come to suppuration, at times the parts remain inflamed and painful for months but no suppuration develops.

Pyosis blastomycetica

This type is closely allied to Furunculosis blastomycetica. The lesions are superficial: papulo vesicles and pustules are present and later crusty impetegoid lesions; removing the crusts shallow ulcers are often seen or occasionally granulating patches. The fungi belong usually to the genus *Monilia*.

(6) *Cryptococcosis epidermica*

Synonym: Blastomycosis epidermica

Remarks. Blastomycosis epidermica was described by me in Ceylon some years ago. Clinically, it has nothing to do with the usual type of blastomycosis, but it may be called blastomycosis, as it is caused by a yeast-like organism.

Synonym. Saccharomyces epidermica, Cryptococcus epidermica.

History and geographical distribution. While in Ceylon, I noticed on the skin of one of my bungalow servants several brownish, dirty-looking patches, which looked very much like dirt. He told me, however, that they did not disappear when soap was used. I made scrapings and saw that these patches consisted of a large number of budding cells which I believed to be saccharomyces. I found the same patches not only in other natives but also in Europeans, especially on the chest and arms, and I called the condition "saccharomycosis epidermica." I did not succeed in growing the fungus. Chalmers and others confirmed my observations in the Sudan and North Africa, but the organism has not yet been cultivated.

Etiology. The causal organism is *Cryptococcus epidermididis* Castellani, 1914.

Symptomatology. The condition is fairly frequent in natives and Europeans who have resided for some years in the tropics. It is characterized by the presence on the arms, and more rarely on the chest and neck, of small, roundish, dirty, yellow or brownish patches, which can generally be removed by thorough scraping. These patches consist of large numbers of blastomyces-like elements of various sizes, rounded or oval, which, so far, have not been cultivated.

Clinical varieties of blastomycosis epidermica. Blastomycosis (cryptococcosis) epidermica, alba and rosea; white patches, consisting solely of yeast-like fungi, without inflammatory signs, are occasionally seen, especially in natives. I have grown the fungi several times; they belong to the genera *Cryptococcus, Saccharomyces* and *Monilia.* In a case with pinkish patches, a

cryptococcus was present which when cultivated on laboratory media gave rise to pink colonies.

FIG. 19. *Cryptococcosis epidermica*

Intertrigo cryptococcica vel moniliaca, Intertrigo blastomycetica and Dermatitidis blastomycetica interdigitalis

Synonyms. Intertrigo saccharomycetica, intertrigo cryptococcica, intertrigo moniliaca.

Intertrigo blastomycetica was first described by me in Ceylon

FIG. 20. CRYPTOCOCCUS FOUND IN *Cryptococcosis epidermica*

in 1907. In Europeans, the affected skin—usually the skin of the inguinal region—is reddened, and there may be a slight exudation. The border of the eruption may be fairly well marked, but it is not distinctly raised. In many cases there is not much itching. In 1907, in scrapings, I found a yeast-like fungus which I called *Saccharomyces samboni*. In other cases I found organisms of the genera *Monilia* and *Cryptococcus*. In recent years a similar condition, saccharomycosis or blastomycosis interdigitalis, has been described by several observers, and I have seen some cases myself and Pollaci has called one of the cryptococcus-like fungi found in it *C. interdigitalis*. In the majority of my cases an epidermophyton was present in addition to numerous yeast-like bodies, that is, in superficial scrapings only yeast-like organisms were present, while in deep scrapings the yeast-like fungus disappeared or was extremely scanty and an epidermophyton was present.

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